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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/382,837	08/25/1999	GARY E. BORODIC	BORO-101	5738

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	19

DATE MAILED: 08/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

10/20/02

10/2 wrong claims
why 11?
why not 14?

15-75

Claim 26 rejected?

Office Action Summary

Application No.	Applicant(s)
09/382,837	Borodic, G.E.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *3/26/02 and 6/4/02* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19 and 21-23* is/are pending in the application.

4a) Of the above, claim(s) *9 and 13-16* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10-12, 17-19, and 21-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/26/02 has been entered.

2. A restriction requirement was set forth in Paper No.3, mailed 1/26/01. Upon reconsideration, Groups III and IV were previously rejoined with elected Group I.

Accordingly, Claims 1-8, 10-12, 17-19, and 21-23 are being acted upon.

3. Claims 9 and 13-16 stand withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

5. New corrected drawings must be filed with the proper changes incorporated therein. See the PTO Form-948 mailed 7/05/01. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top

margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Corrections other than Informalities Noted by Draftsperson on form PTO-948. All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections. Note that the filing of corrected drawings may no longer be held in abeyance until such time as claims are found allowable. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

6. The declaration is objected to because it claims priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846 as indicated in the first line of the specification. A new declaration is required.

In Paper No. 12, filed 11/05/01, Applicant has indicated that a new declaration will be submitted.

7. In view of Applicant's amendment and response, filed 3/26/02, the rejections of Claims 2 and 4, under the second paragraph of 35 U.S.C. 112, and Claim 5, under the first paragraph of 35 U.S.C. 112 have been withdrawn.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 17-19 and 21-23 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record as set forth in Papers No. 13 and 11, mailed 1/09/02 and 7/05/01, respectively. This is a new matter rejection.

Applicant's arguments, filed 3/26/02, have been fully considered but they are not persuasive. Applicant argues the support for "a method of treating neurogenic inflammation" and "at least one neurogenic inflammatory mediator" can be found throughout the specification, and cites four examples. Applicant further argues that "Indeed, one of ordinary skill in the art, when reading the specification as a whole, would understand that the invention encompasses the treatment of neurogenic inflammation and the antagonism of at least one neurogenic mediator. All of the extensive discussion throughout the specification of mast cell and nerve cell release of "preformed mediators" and the blockage of such release by chemodenervating pharmaceuticals, such as botulinum toxin, would be clearly understood by one of ordinary skill in the art as referring to neurogenic inflammation and neurogenic mediators". It remains the Examiner's position that Applicant has attempted to redefine the invention of the instant claims. First, note that of the four examples cited by Applicant, only "[I]nflammation in torticollis in peripheral tissues may be neurogenically mediated," comprises a reference to the term neurogenic. But even this example includes the word *may*, indicating that Applicant is not specifically disclosing a method comprising a neurogenic process, and the cite fails to disclose that the method of the instant claims functions through a specific interaction with this possible process. Second, a careful reading of the specification shows that the invention of the instant claims functions through an interruption of the release of preformed mast cell mediators, particularly histamine (see for example page 5, paragraph 1, and page 6, paragraph 2). Neurogenic inflammation, however, comprises a number of

interactions including interactions between the nervous system and keratinocytes, Langerhans cells, dermal microvasculature endothelial cells, infiltrating immune cells, *and* mast cells. Further, neurogenic inflammation comprises a component of conditions/diseases ranging from psoriasis to contact dermatitis (see Scholzen et al., 1998). Except for that with mast cells, these interactions are not disclosed in the specification, nor are many of the conditions/diseases that the method would now encompass treatments for. Accordingly, it remains the Examiner's position that the specification cannot support claims amended to recite a method of treating neurogenic inflammation.

Applicant continues with an argument that the specification of U.S. Patent No. 6,063,768 would lead one of skill in the art to understand that the instant disclosure refers specifically to neurogenic inflammation. The Examiner fails to understand the logic of the argument. While both the '768 patent and the instant application teach a method of administering botulinum toxin, Applicant's argument that what is disclosed in the '768 patent must therefore be considered to be disclosed in the instant application is simply improper, particularly in light of the fact that the '768 patent was not issued until after the filing date of the instant application, thus the disclosure therein was not public information at the time of the filing of the instant application.

Applicant cites a number of other references teaching neurogenic inflammation, and further argues that the specific teachings of the references should be considered to be encompassed by the instant application. It remains the Examiner's position however, that the vague disclosures of the instant specification cannot now be considered to encompass the specific teachings of the prior art. For example, the disclosure of a genus (e.g., cytokine) is insufficient to support a claim drawn to a species (e.g., interleukin 1). Specifically, a disclosure of "preformed mediators which result in vascular dilation" is insufficient to support a claim drawn to substance P or many of the other specific mediators of Claim 19. Note that substance P is disclosed only in the title of a cited reference and not as a neurogenic inflammatory mediator as claimed in Claim 19. Other specific mediators, such as interleukin 1 and calcitonin gene-related peptide, are not disclosed at all. Likewise, the disclosure of "an anti-inflammatory agent which is injected directly into joints" is insufficient support for Claim 22 reciting a method of treating gout.

Regarding Claim 23, it is not the recitation of "histamine"

that the specification cannot support, but rather the recitation of "neurogenic inflammation."

10. Claims 2-4 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of reducing allergy induced conjunctivitis in a mouse comprising administering a botulinum toxin,

does not reasonably provide enablement for:

A) a method of reducing inflammation without causing muscle weakness,

B) a method of reducing inflammation comprising an effective dose of botulinum toxin less that 2.5 units,

for the reasons of record as set forth in Papers No. 13 and 11, mailed 1/09/02 and 7/05/01, respectively.

Applicant's arguments, filed 3/26/02, have been fully considered but they are not persuasive. Applicant argues that the example disclosing the treatment of spasmodic torticollis supports the claims. However, it is noted that: a)muscle weakness was not measured and b) a specific dosage is not disclosed (only a range of 0.6 to 15 units which cannot support the recitation of Claim 4 (below 2.5 botulinum units). Applicant further argues that the example entitled "Conjunctivitis" supports the method of the instant claims. Again, however, muscle weakness was not measured.

11. The instant application claims the benefit of priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846. Claims 1-8 and 10-12 are granted said benefit of priority. However, the '846 application does not teach a method for treating neurogenic inflammation. Accordingly, 17-19 and 21-23 are denied the benefit of priority. The priority date of said claims is the filing date of the instant application, 8/25/99.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 3c of this title before the invention thereof by the applicant for patent.

13. Claims 1, 5-6, and 17-23 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,063,768 (filed 9/04/97), for the reasons of record as set forth in Papers No. 13

and 11, mailed 1/09/02 and 7/05/01, respectively.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1, 5-8, 10-12, and 17-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,063,768 (filed 9/04/97)) in view of The Merck Manual (1992) for the reasons of record as set forth in Papers No. 13 and 11, mailed 1/09/02 and 7/05/01, respectively.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

16. Applicant's request that an interference be declared between the instant application and U.S. Patent No. 6,063,768 is again acknowledged. However, no interference shall be established until such time as all pending claims are found allowable **and** Applicant has submitted appropriate evidence showing entitlement to said declaration.

17. The following are new grounds for rejection>

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 15-6 and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) the recitation of "includes" in Claims 5 and 12 is vague and indefinite as it is impossible to establish the metes and bounds of the claims. Applicant is advised that the amending of the term to the more definite "is" or "are" would obviate the rejections,

B) In Claim 6 "an other" is properly "another".

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
August 23, 2002